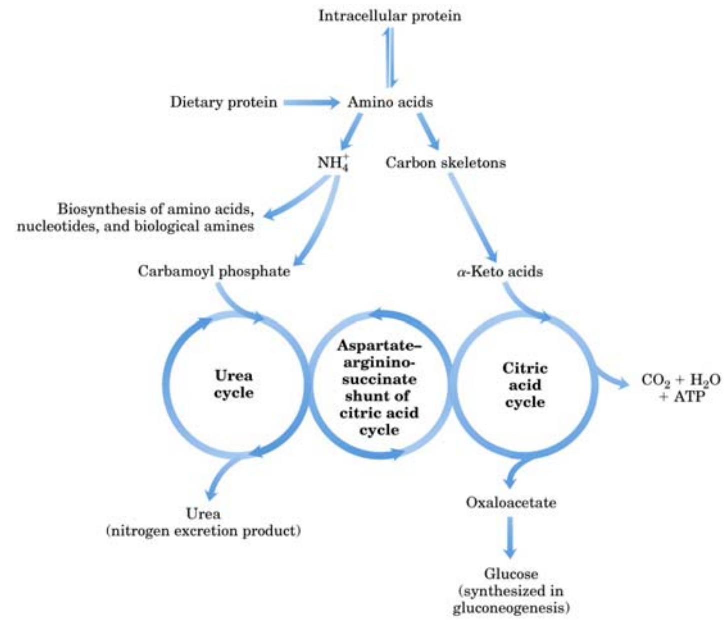
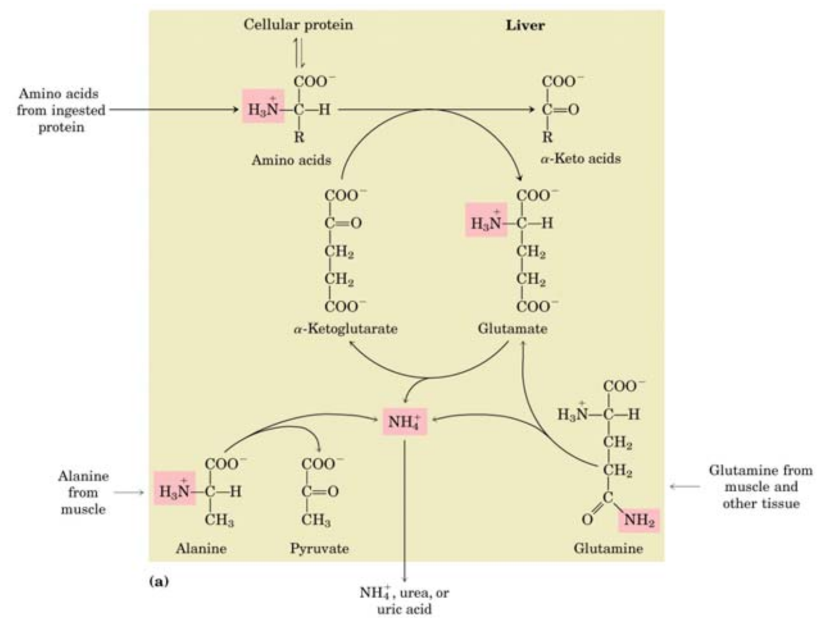
Amino Acid Oxidation

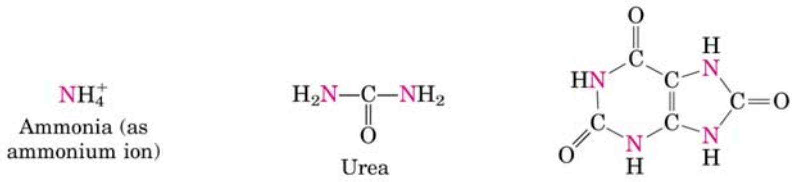
- Protein turnover
- High protein diet
- Starvation/diabetes



Three aspects of AA oxidation

- Amino group metabolism
- Nitrogen excretion
- Fate of C skeletons obtained from AAs





Ammonia (as ammonium ion)

Urea

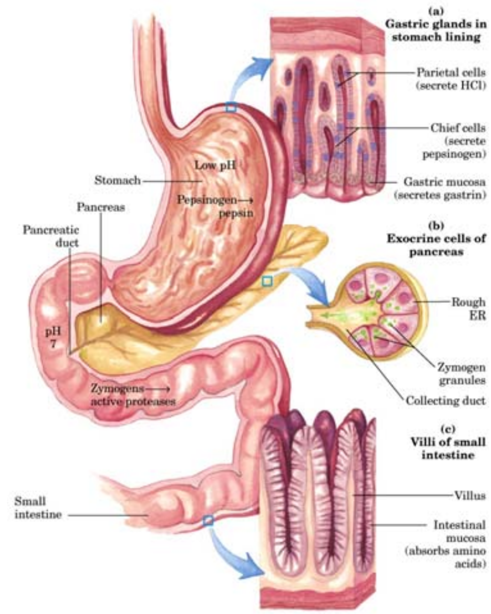
Uric acid

Ammonotelic animals: most aquatic vertebrates, such as bony fishes and the larvae of amphibia

Ureotelic animals: many terrestrial vertebrates; also sharks

Uricotelic animals: birds, reptiles

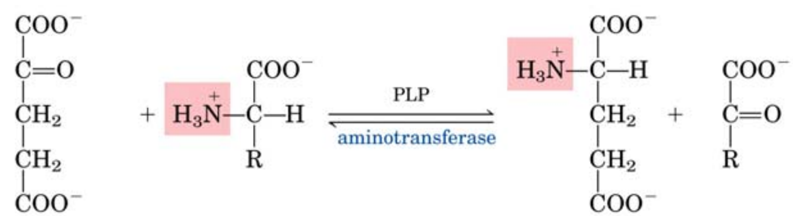
(b)



Reactions involving amino group transfer

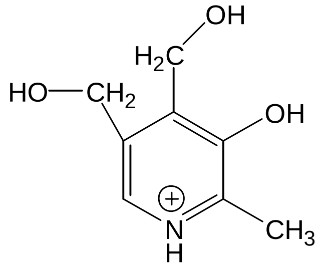
- Transamination
- Oxidative deamination
- Hydrolytic deamination
- ATP-dependent amination

Transamination

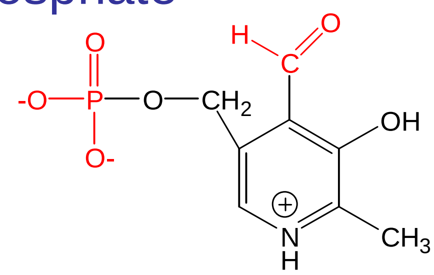


α-Ketoglutarate L-Amino acid L-Glutamate α-Keto acid

Vitamin B_6 and Pyridoxal phosphate

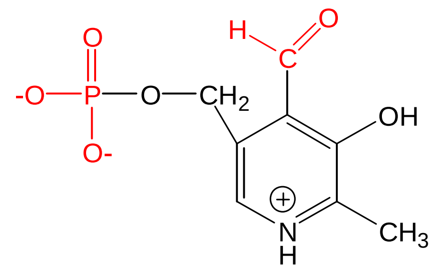


Vitamin B_6
Pyridoxine
pyridoxol

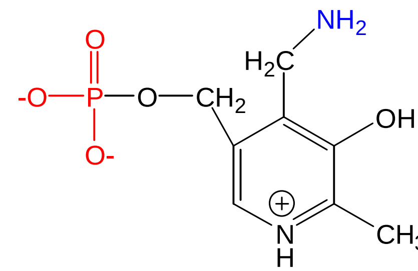


Pyridoxal phosphate

Pyridoxal phosphate and Pyridoxamine

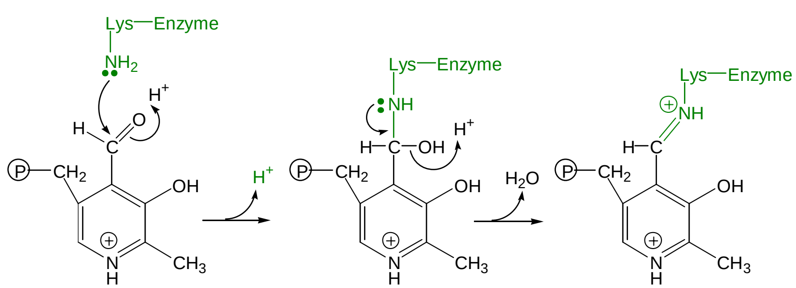


Pyridoxal phosphate



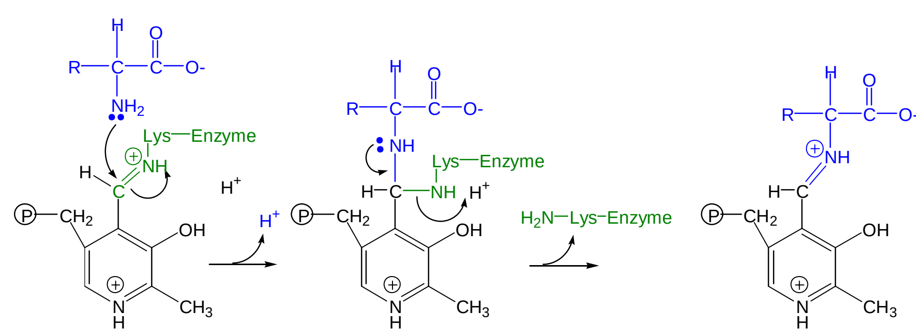
Pyridoxamine phosphate

Formation of the Schiff base adduct of PLP and the ε-amino group of a lysine side chain

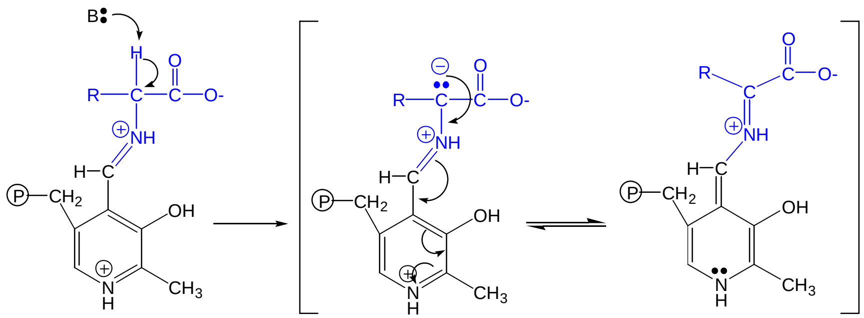


"aldimine" adduct

Reaction of the "internal" aldimine with a free amino acid to produce an "external" aldimine

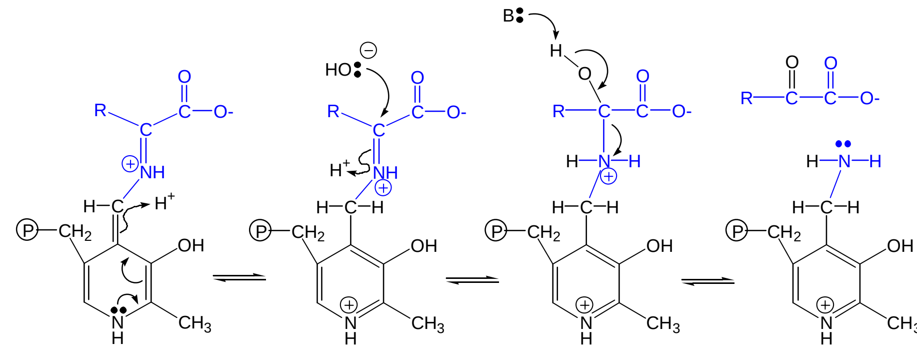


Abstraction of the α proton of the amino acid substrate



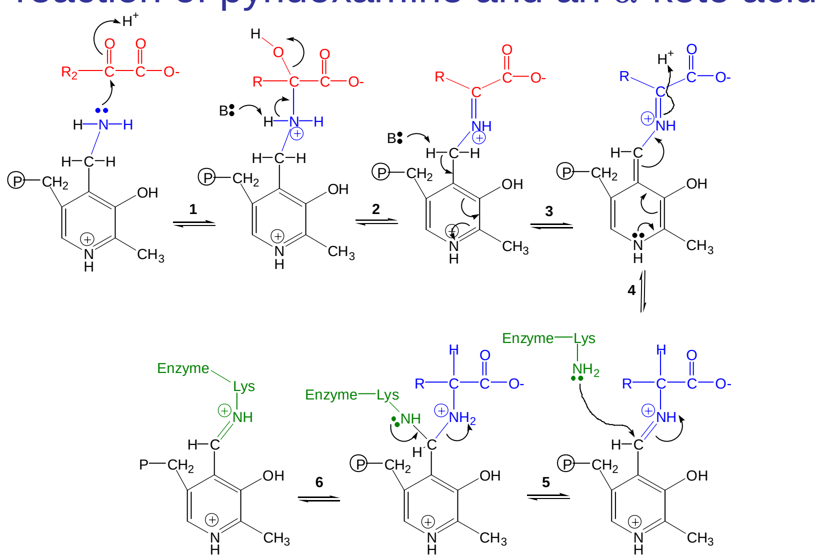
aldimine α-carbanion Resonance stabilized carbanion

The first half reaction of transamination: formation of pyridoxamine and an α-keto acid

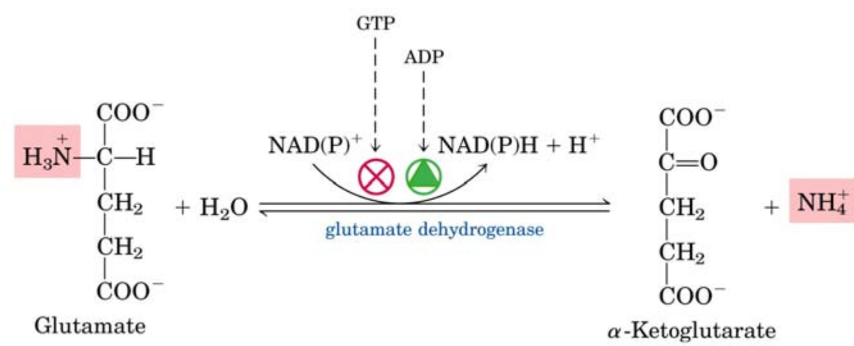


stabilized carbanion ketimine carbinolamine pyridoxamine

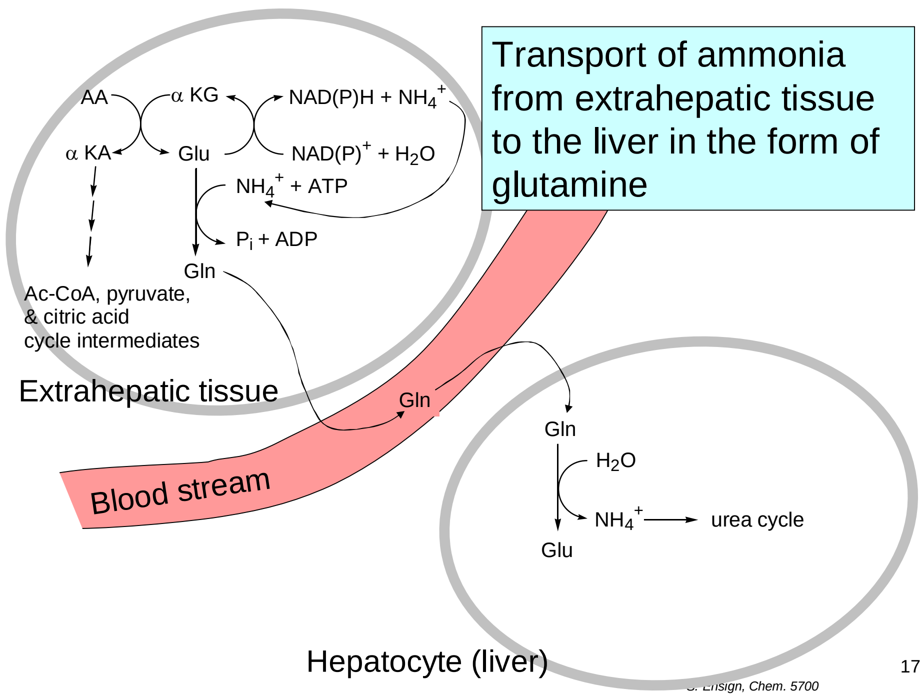
The second half reaction of transamination: reaction of pyridoxamine and an α-keto acid

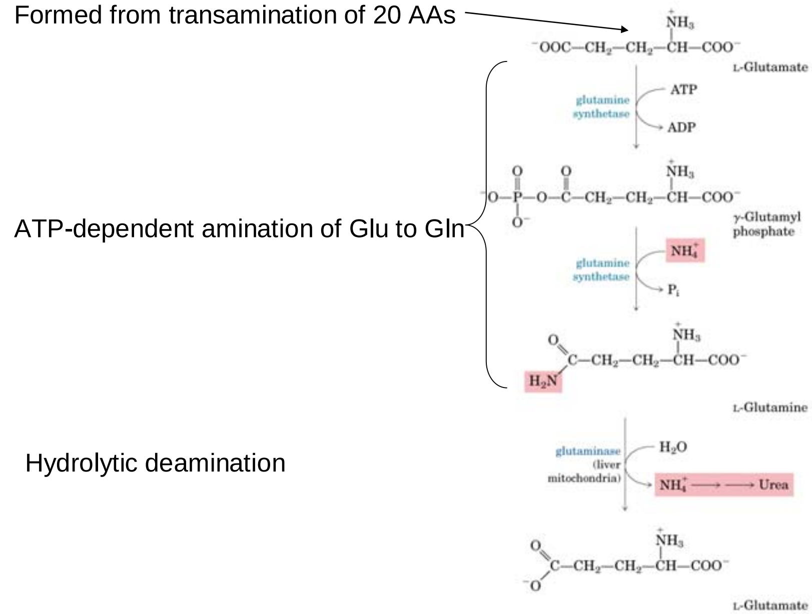


Oxidative deamination

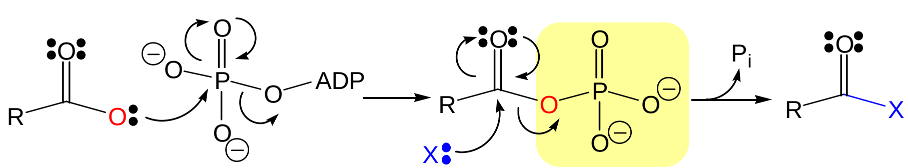


Transport of ammonia from extrahepatic tissue to the liver in the form of glutamine

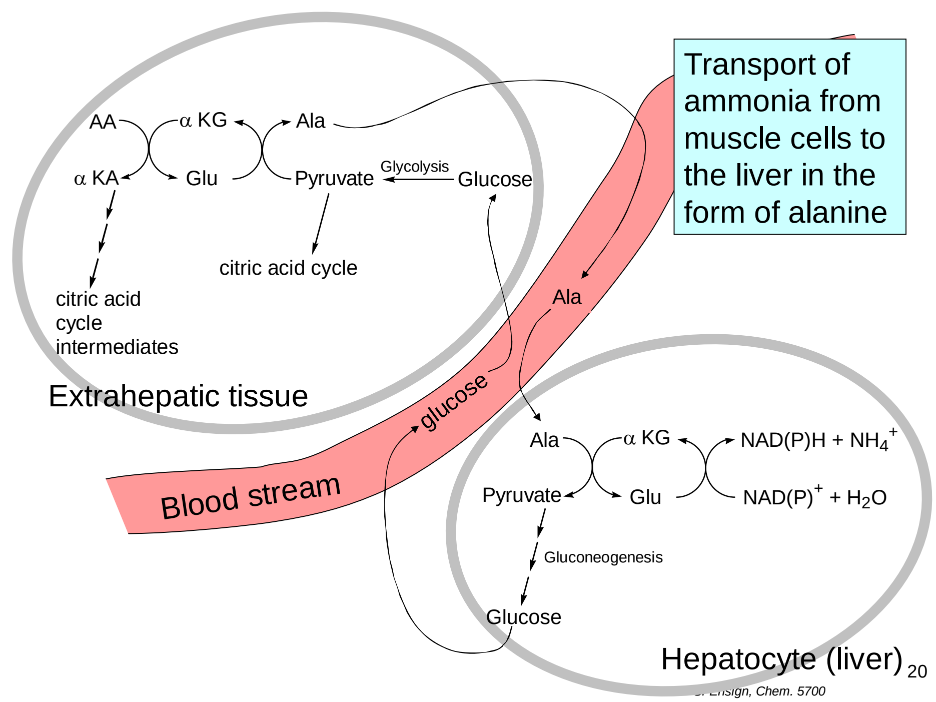




Nucleophilic displacement reactions often require activation of a poor leaving group to a good leaving group by addition of phosphate from ATP



Transport of ammonia from muscle cells to the liver in the form of alanine



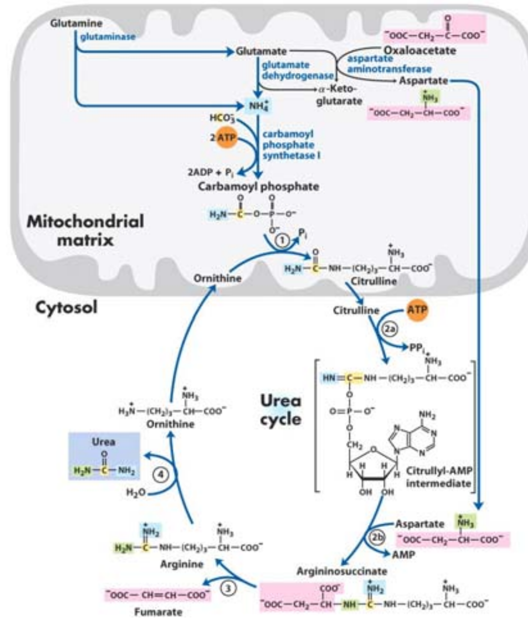
What are the α-keto acid counterparts for the following amino acids?

Alanine

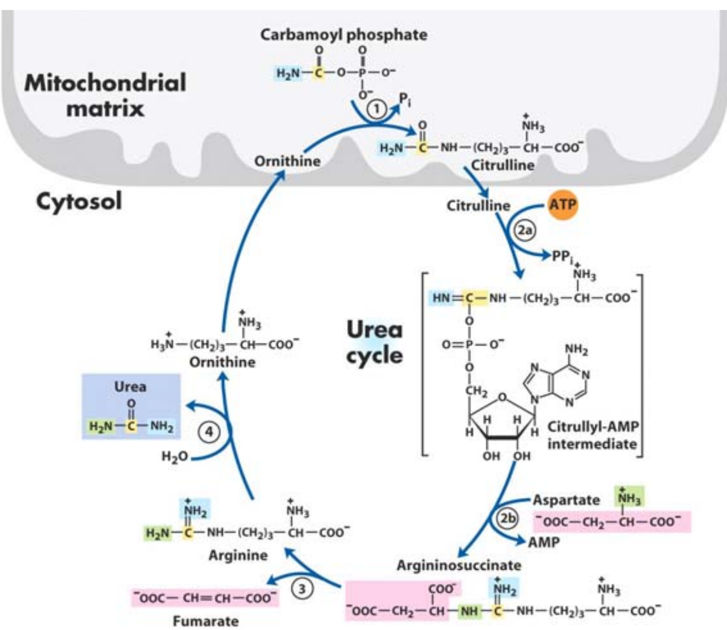
Aspartate

Glutamate

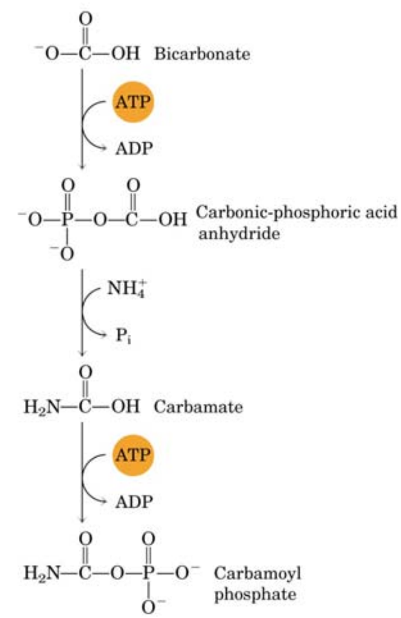
Nitrogen Excretion and The Urea Cycle



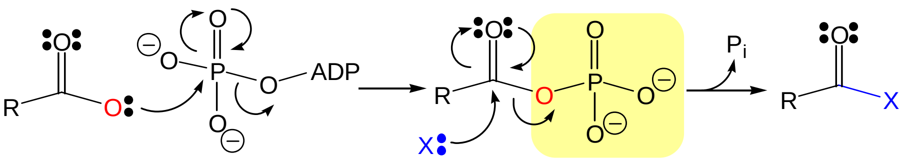
The Urea Cycle



Formation of carbamoyl phosphate: carbamoyl phosphate synthetase



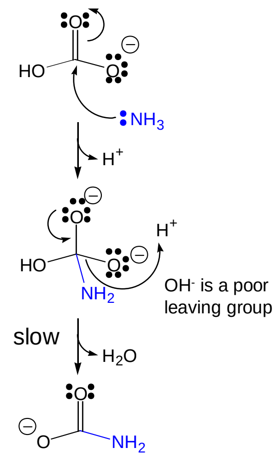
Nucleophilic displacement reactions often require activation of a poor leaving group to a good leaving group by addition of phosphate from ATP



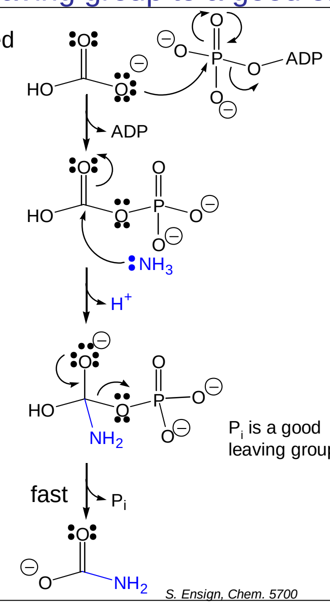
Carbamoyl phosphate synthetase

Role of ATP in converting a poor leaving group to a good one

Uncatalyzed amination (first part of reaction):

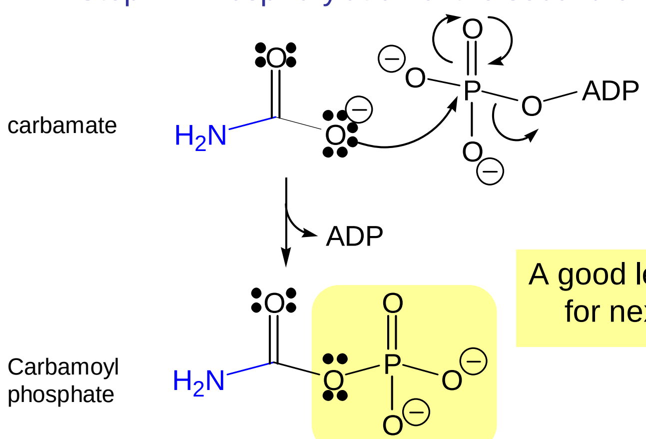


ATP-assisted amination (first part of reaction):



Carbamoyl phosphate synthetase

Step 2: Phosphorylation of the second oxygen

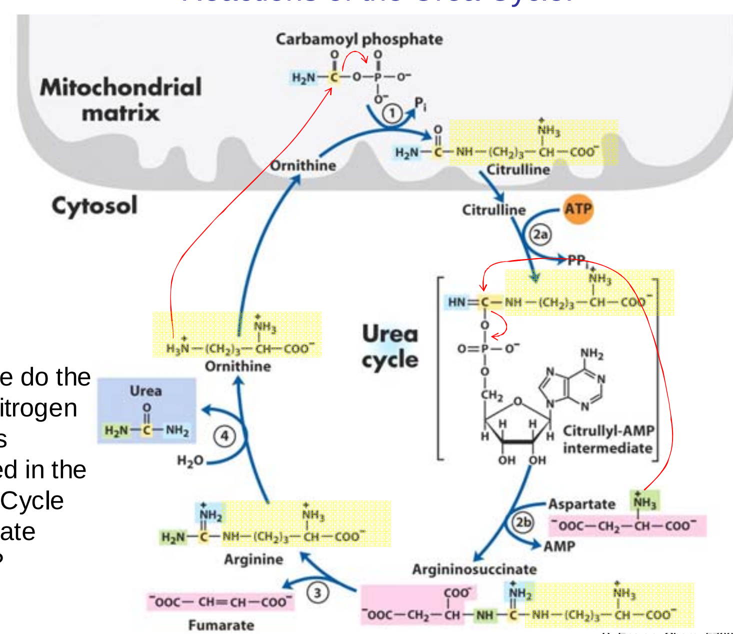


A good leaving group for next reaction

Overall reaction: $HCO_3^- + 2ATP + NH_3 \rightarrow$ carbamoyl phosphate + P_i

Reactions of the Urea Cycle:

Where do the two nitrogen atoms formed in the Urea Cycle originate from?



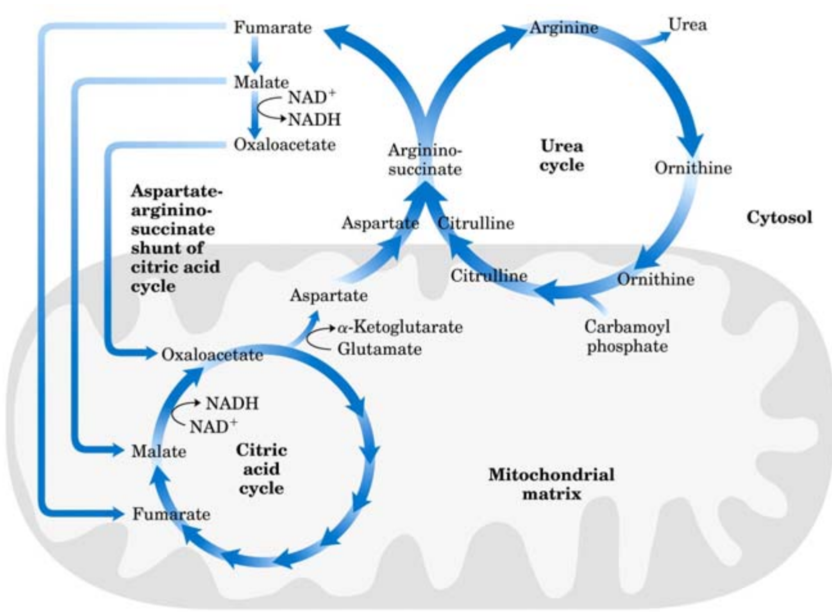
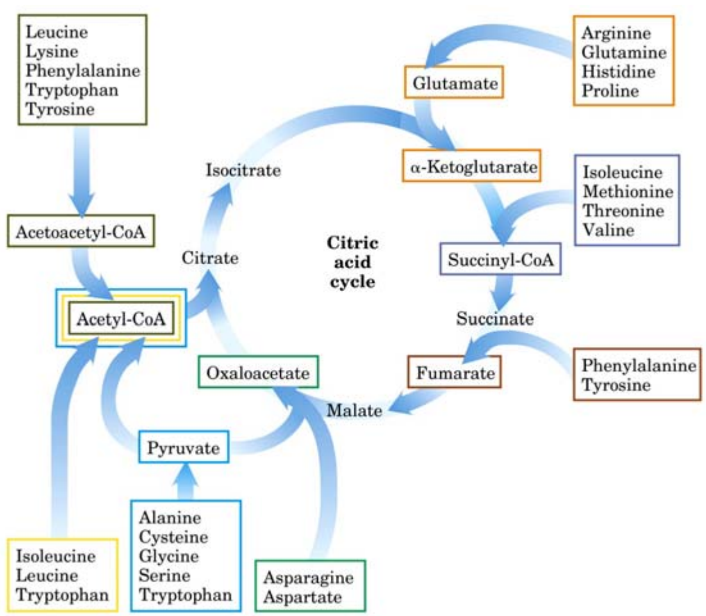


table 18–1

Nonessential and Essential Amino Acids for Humans and the Albino Rat

Nonessential	Essential
Alanine	Arginine*
Asparagine	Histidine
Aspartate	Isoleucine
Cysteine	Leucine
Glutamate	Lysine
Glutamine	Methionine
Glycine	Phenylalanine
Proline	Threonine
Serine	Tryptophan
Tyrosine	Valine

*Essential in young, growing animals but not in adults.



C-1 metabolism

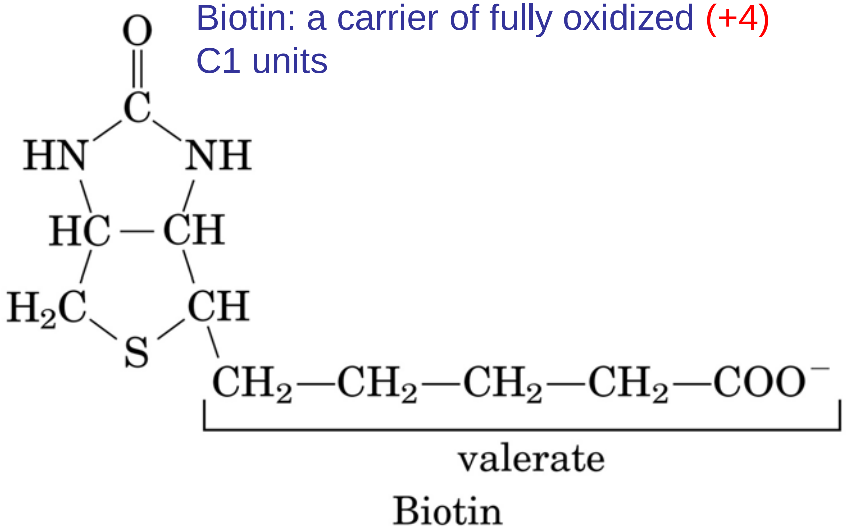
Biologically important oxidation states of C1 compounds

Oxidation state	Representative C1 molecules
+4	HCO_3^-, CO_2
+2	HCOOH, CO
0	HCOH
-2	CH_3OH
-4	CH_4

Why do we need C1 group carriers?? i.e., why not have these molecules as free metabolites, like pyruvate or citrate?

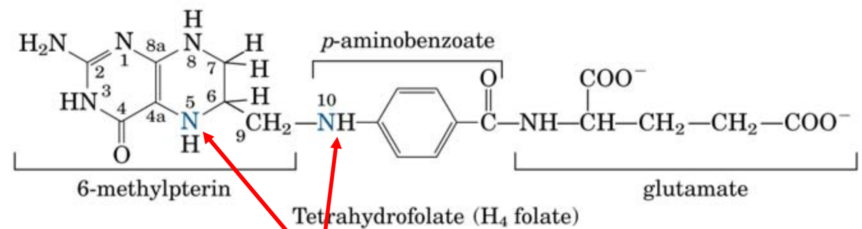
Cofactors of one-carbon transfer

Biotin: a carrier of fully oxidized (+4) C1 units

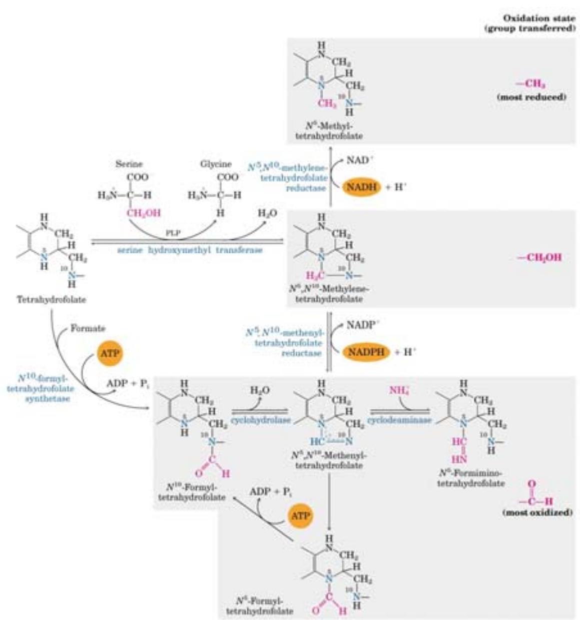


Cofactors of one-carbon transfer

Tetrahydrofolate: a carrier of diverse C1 units at 3 different oxidation levels (+2, 0, -2)



Sites(s) of C1 group attachment



Formal oxidation state of C1 unit

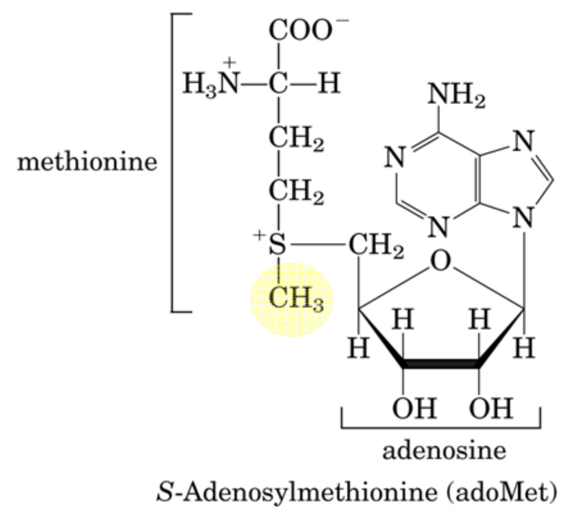
-2

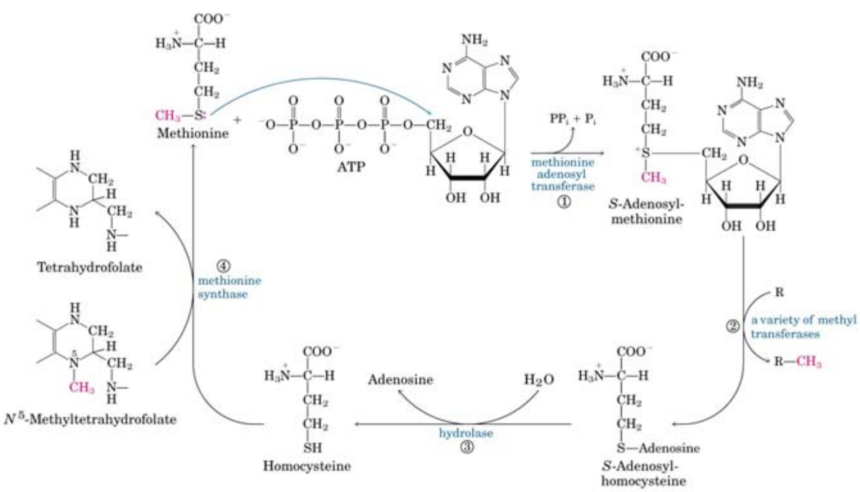
0

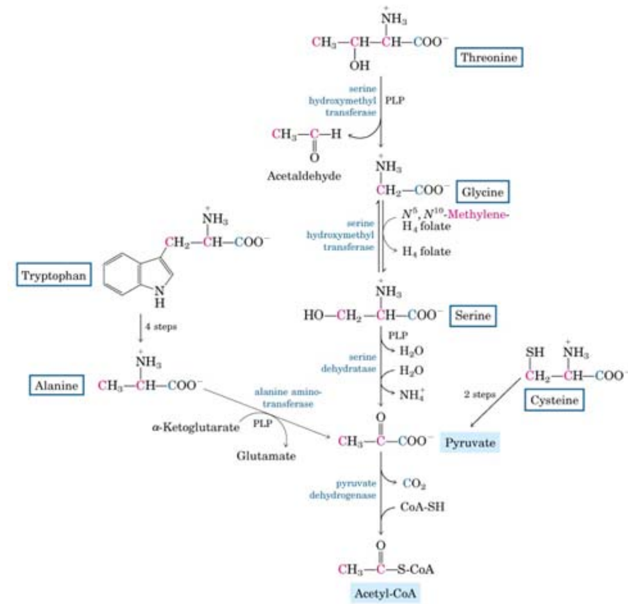
+2

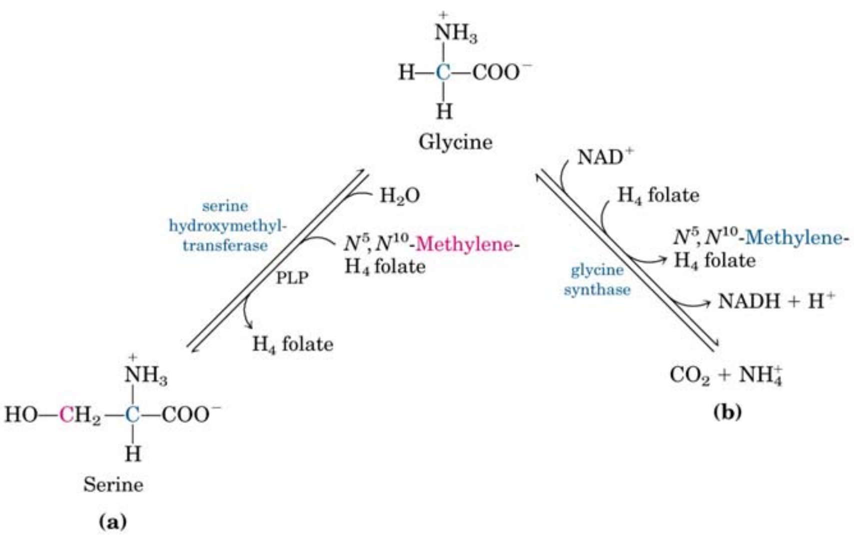
Cofactors of one-carbon transfer

SAM: a carrier of a C1 methyl unit (-2)









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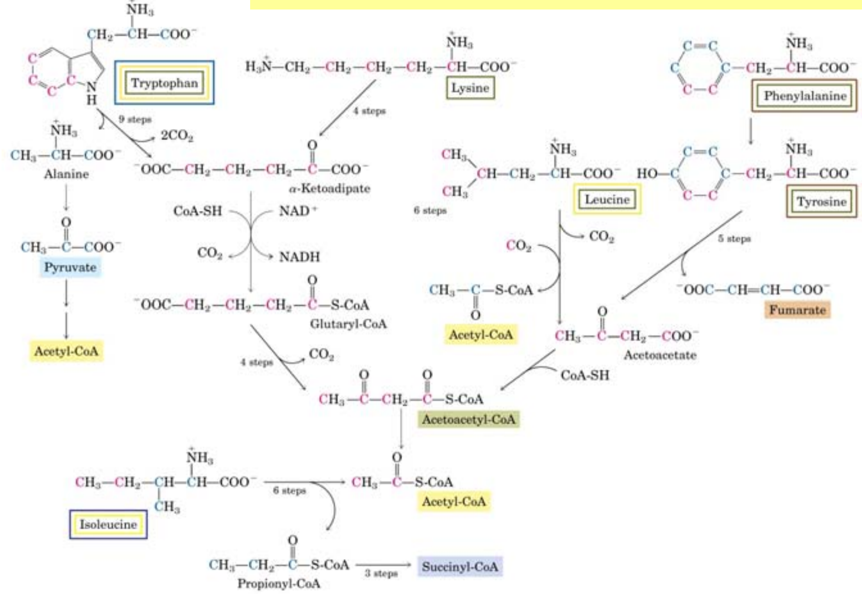

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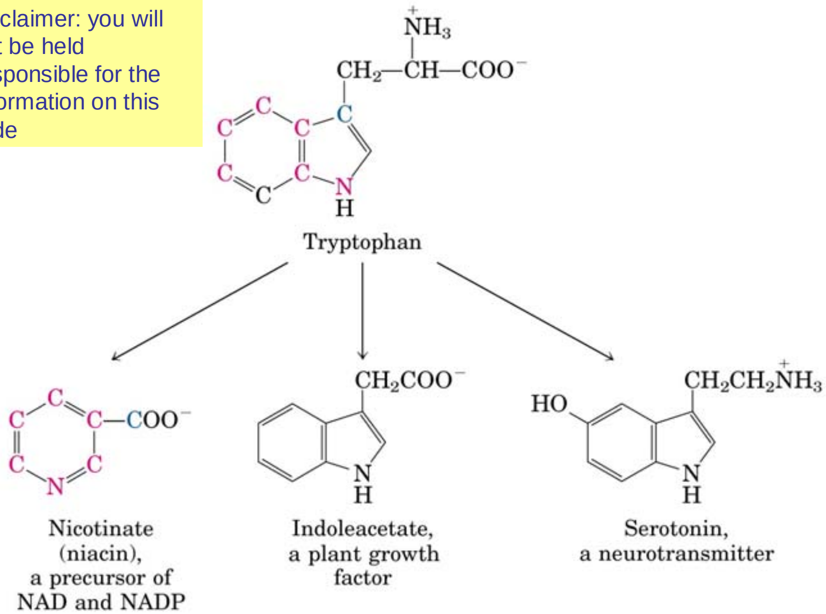

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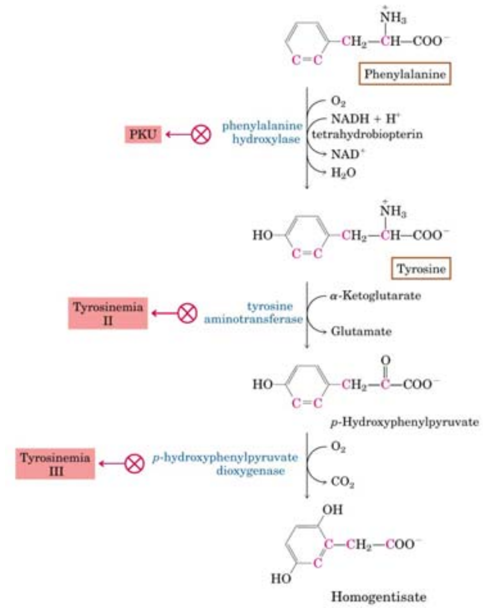

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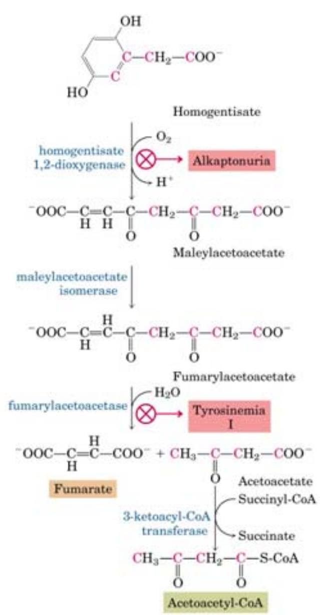

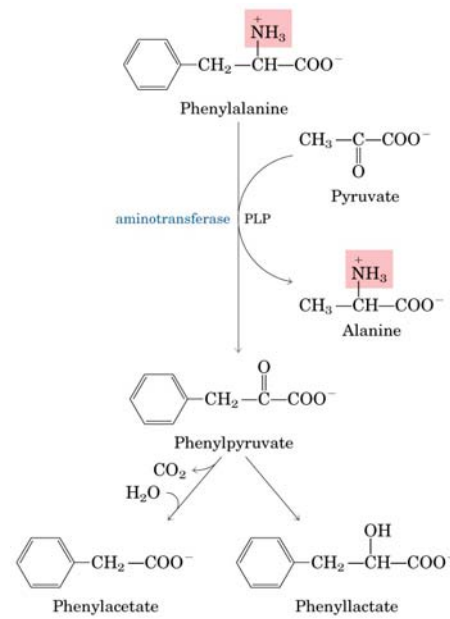

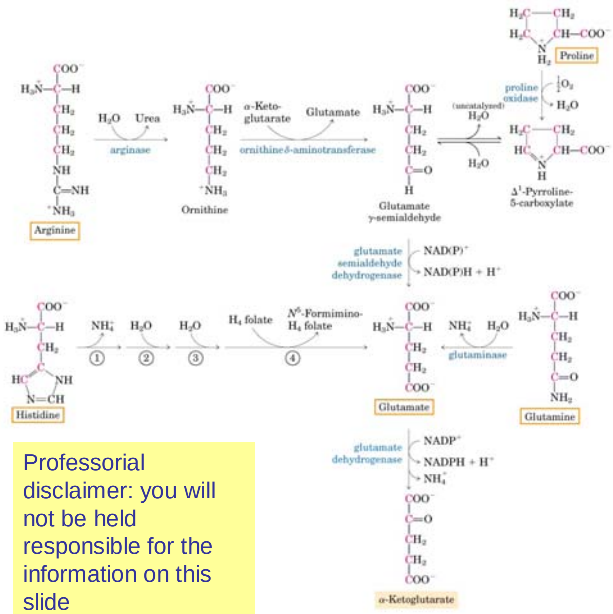

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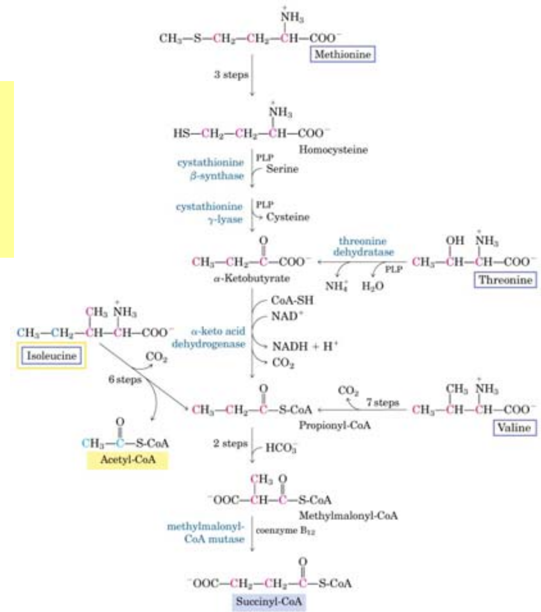

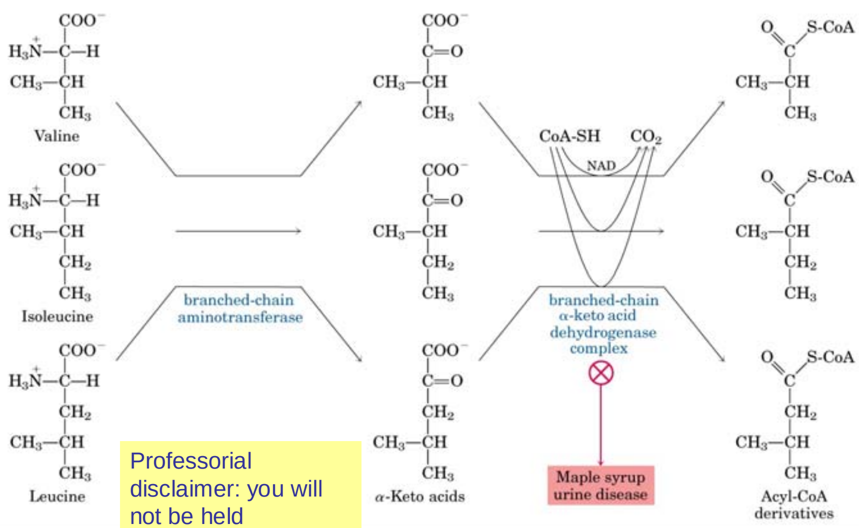

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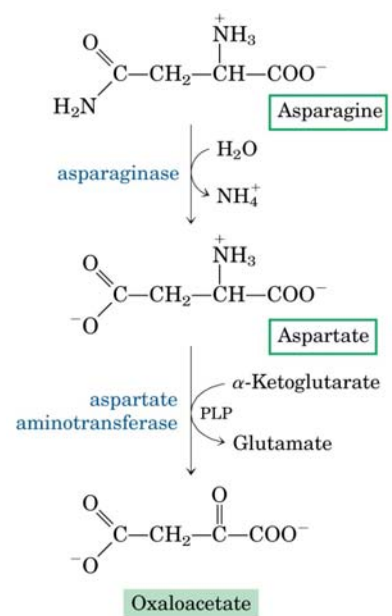

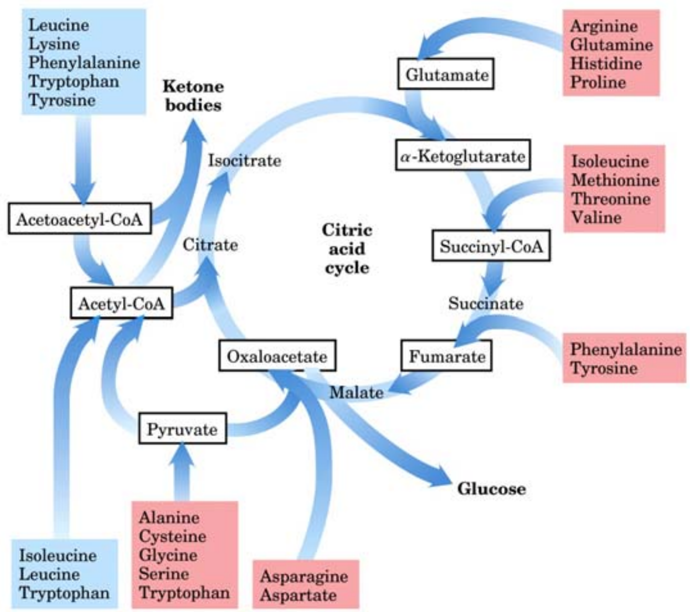
Leucine
Lysine
Phenylalanine
Tryptophan
Tyrosine
Ketone bodies
Acetoacetyl-CoA
Acetyl-CoA
Isocitrate
Citrate
Citric acid cycle
Glutamate
Arginine
Glutamine
Histidine
Proline
α-Ketoglutarate
Isoleucine
Methionine
Threonine
Valine
Succinyl-CoA
Succinate
Fumarate
Phenylalanine
Tyrosine
Malate
Oxaloacetate
Pyruvate
Glucose
Isoleucine
Leucine
Tryptophan
Alanine
Cysteine
Glycine
Serine
Tryptophan
Asparagine
Aspartate